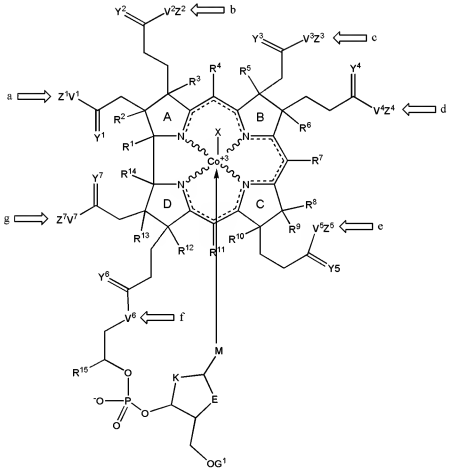
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Collins, et al.	Art Unit	: 1623
Serial No.	: 10/028,857	Examiner	: Leigh C. Maier
Filed	: October 25, 2001	Conf. No.	: 9356
Title	: TRANSCOBALAMIN RECEPTOR BINDING CONJUGATES FOR NEUTRON CAPTURE THERAPY		

PENDING CLAIMS

1. (Currently amended) A compound of formula (**I**):



or its enantiomer, diastereomer or its pharmaceutically acceptable salt, wherein:

(i) the wavy line in the chemical structure indicates either a dative or covalent bond such that there are three dative Co-N bonds and one covalent Co-N bond,

wherein, the case of the dative bond, the valence of nitrogen is completed either with a double bond with an adjacent ring carbon or with a hydrogen;

(ii) the dotted line in the chemical structure indicates either a double or single bond such that the double bond does not over-extend the valence of the element (i.e. to give pentavalent carbons) and, in the case of a single bond, the valence is completed with hydrogen;

(iii) X is hydrogen, cyano, halogen ~~(Cl, F, Br or I)~~, haloalkyl, CF_3, CF_2CF_3, CH_2CF_3, CF_2Cl, NO, NO_2, NO_3, phosphonate, alkyl-$P(O)_2OR^{15}$, $PR^{15}R^{16}R^{17}$, NH_2, $NR^{15}R^{16}$, OH, OR^{15}, SR^{15}, SCN, N_3, $OC(O)R^{15}$, $C(O)_2R^{15}$, $C(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $C(O)_2NR^{15}R^{16}$, $C(O)NR^{15}R^{16}$, $P(O)_2OR^{15}$, $S(O)_2OR^{15}$, a purine or pyrimidine nucleoside or nucleoside analog, adenosyl, 5-FU, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, amino acid, peptide, protein, carbohydrate, heteroalkyl, heterocycle, heteroaryl or alkylheteroaryl;

(iv) M is a monovalent heterocycle or heteroaromatic, which is capable of binding to the adjacent sugar ring, and forming a dative bond with Co^{+3};

(v) K is O, S, NJ^1, C(OH)H, $CR^{100}R^{101}$ or $C(R^{100})V^8Z^8$;

(vi) E is O or S;

(vii) G^1 is ~~hydrogen,~~ alkyl, acyl, silyl, phosphate or L-T;

(viii) Y^1, Y^2, Y^3, Y^4, Y^5, Y^6 and Y^7 independently are O, S or NJ^2;

(ix) V^1, V^2, V^3, V^4, V^5, V^6, V^7 and V^8 independently are O, S, NJ^3, $CR^{102}R^{103}$ or a direct bond;

(x) Z^1, Z^2, Z^3, Z^4, Z^5, Z^7 and Z^8 independently are R^{104} or L-T;

(xi) each L is independently a direct bond or linker to one or more T moieties, and that does not significantly impair the ability of the TC- or IF-binding carrier to bind to a transcobalamin receptor, optionally when bound to a transport protein;

(xii) each T independently comprises the residue of one or more molecules of neutron capture agents;

(xiii) at least one of Z^1, Z^2, Z^3, Z^4, Z^5, Z^7, and Z^8~~, K and G~~ is L-T;

(xiv) J^1, J^2 and J^3 independently are hydrogen, alkyl, alkenyl, alkynyl, alkaryl, cycloalkyl, aryl, cycloaryl, heteroalkyl, heterocycle, heteroaryl, hydroxyl, alkoxy or amine;

(xv) R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} independently are hydrogen, lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, heteroalkyl, heterocyclic, lower alkoxy, azido, amino, lower alkylamino, halogen, thiol, SO_2, SO_3, carboxylic acid, $C_{1\text{-}6}$ carboxyl, hydroxyl, nitro, cyano, oxime or hydrazine;

(xvi) R^{13} and R^{14} optionally can form a double bond;

(xvii) R^{15}, R^{16} and R^{17} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkaryl or aralkyl group, heteroalkyl, heterocycle or heteroaromatic; and

(xviii) R^{100}, R^{101}, R^{102}, R^{103}, and R^{104} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, acyl, heteroaromatic, heteroaryl, heteroalkyl, hydroxyl, alkoxy, cyano, azido, halogen, nitro, SO_2, SO_3, thioalkyl or amino;

(xix) wherein ~~at least one of each E,~~ G^1 ~~, K, M, R, V and Y~~ is ~~independently~~ not as it is found in natural vitamin B_{12}.

2. (Currently amended) The compound of claim 1, wherein at least one T is a molecule ~~that contains~~ comprising B-10.

3. (Original) The compound of claim 2, wherein the molecule that contains B-10 is o-carborane, m-carborane or p-carborane.

4. (Currently amended) The compound of claim 1, wherein at least one T is a molecule ~~that contains~~ comprising Gd-157.

5. (Currently amended) The compound of any one of claims 1-4, wherein at least one L is independently an amine, a polyamine, an amino acid, a poly(amino acid) or peptide ~~linker;~~ linker.

6. (Original) The compound of any one of claims 1-4, wherein at least one –L-T is independently a poly(amino acid) residue bound to one or more T.

7. (Original) The compound of claim 6, wherein at least one –L-T is independently a poly-L-lysine -NR'(CH((CH_2)$_4$-NHR')CONR')$_m$R', wherein each R' is independently hydrogen, lower alkyl or T; and m is 2-20.

8. (Currently amended) The compound of any one of claims 1-4, wherein at least one –L-T is independently a polyamine residue of the formula -NR'(alkylene-NR')$_n$alkyleneNR'R', wherein each R' is independently hydrogen, lower alkyl ~~or T~~ or T; and n is 1-20.

9. (Original) The compound of claim 8, wherein -NR'(alkylene-NR')$_n$alkyleneNR' is selected from the group consisting of -NR'(CH_2)$_3$NR'(CH_2)$_4$NR'(CH_2)$_3$NR'R'

(spermine); -NR'$(CH_2)_3$NR'$(CH_2)_4$NR'R' (spermidine); decamethylene tetraamine and pentamethylene hexamine.

10. (Currently amended) The compound of any one of claims 1-4, wherein at least one –L-T is independently a diamine residue of the formula -NR'(alkylene)$_x$NR'R', wherein each R' is independently hydrogen, lower alkyl ~~or T~~ or T; and x is 2-20.

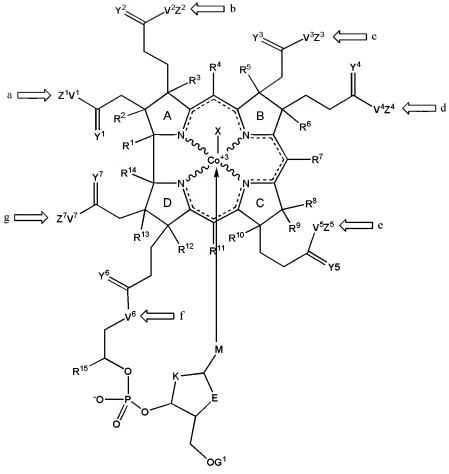
11. (Original) The compound of claim 10, wherein –NR'(alkylene)$_x$NR'R' is selected from the group consisting of 1,6-diaminohexane, 1,5-diaminopentane, 1,4-diaminobutane and 1,3-diaminopropane.

12. (Original) A pharmaceutical composition for the treatment, prophylaxis and/or diagnosis of a proliferative disorder in a host comprising a compound of any one of claims 1-11, or the pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

13. (Original) A pharmaceutical composition for the treatment, prophylaxis and/or diagnosis of a proliferative disorder in a host comprising a compound of any one of claims 1-11, or the pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier, in combination with one or more other therapeutic and/or diagnostic agents(s).

14. (Original) The pharmaceutical composition of claim 12 or 13, wherein the host is a human.

15. (Withdrawn - currently amended) A method for the treatment, prophylaxis and/or diagnosis of a proliferative disorder in a host comprising administering an effective amount of a compound of ~~any one of claims 1-11,~~ formula (I):



or its enantiomer, diastereomer or ~~the~~ pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier, wherein:

(i) the wavy line in the chemical structure indicates either a dative or covalent bond such that there are three dative Co-N bonds and one covalent Co-N bond, wherein, the case of the dative bond, the valence of nitrogen is completed either with a double bond with an adjacent ring carbon or with a hydrogen;

(ii) the dotted line in the chemical structure indicates either a double or single bond such that the double bond does not over-extend the valence of the element (i.e. to give pentavalent carbons) and, in the case of a single bond, the valence is completed with hydrogen;

(iii) X is hydrogen, cyano, halogen, haloalkyl, CF_3, CF_2CF_3, CH_2CF_3, CF_2Cl, NO, NO_2, NO_3, phosphonate, alkyl-$P(O)_2OR^{15}$, $PR^{15}R^{16}R^{17}$, NH_2, $NR^{15}R^{16}$, OH, OR^{15}, SR^{15}, SCN, N_3, $OC(O)R^{15}$, $C(O)_2R^{15}$, $C(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $C(O)_2NR^{15}R^{16}$, $C(O)NR^{15}R^{16}$, $P(O)_2OR^{15}$, $S(O)_2OR^{15}$, a purine or pyrimidine nucleoside or nucleoside analog, adenosyl, 5-FU, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, amino acid, peptide, protein, carbohydrate, heteroalkyl, heterocycle, heteroaryl or alkylheteroaryl;

(iv) M is a monovalent heterocycle or heteroaromatic, which is capable of binding to the adjacent sugar ring, and forming a dative bond with Co^{+3};

(v) K is O, S, NJ^1, C(OH)H, $CR^{100}R^{101}$ or $C(R^{100})V^8Z^8$;

(vi) E is O or S;

(vii) G^1 is alkyl, acyl, silyl, phosphate or L-T;

(viii) Y^1, Y^2, Y^3, Y^4, Y^5, Y^6 and Y^7 independently are O, S or NJ^2;

(ix) V^1, V^2, V^3, V^4, V^5, V^6, V^7 and V^8 independently are O, S, NJ^3, $CR^{102}R^{103}$ or a direct bond;

(x) Z^1, Z^2, Z^3, Z^4, Z^5, Z^7 and Z^8 independently are R^{104} or L-T;

(xi) each L is independently a direct bond or linker to one or more T moieties, and that does not significantly impair the ability of the TC- or IF-binding carrier to bind to a transcobalamin receptor, optionally when bound to a transport protein;

(xii) each T independently comprises the residue of one or more molecules of neutron capture agents;

(xiii) at least one of Z^1, Z^2, Z^3, Z^4, Z^5, Z^7, and Z^8~~, K and G^1~~ is L-T;

(xiv) J^1, J^2 and J^3 independently are hydrogen, alkyl, alkenyl, alkynyl, alkaryl, cycloalkyl, aryl, cycloaryl, heteroalkyl, heterocycle, heteroaryl, hydroxyl, alkoxy or amine;

(xv) R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} independently are hydrogen, lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, heteroalkyl, heterocyclic, lower alkoxy, azido, amino, lower alkylamino, halogen, thiol, SO_2, SO_3, carboxylic acid, $C_{1\text{-}6}$ carboxyl, hydroxyl, nitro, cyano, oxime or hydrazine;

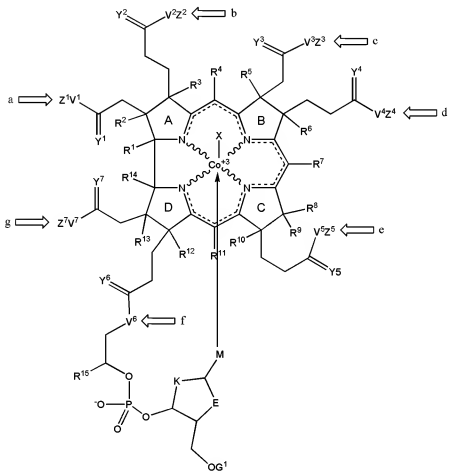
(xvi) R^{13} and R^{14} optionally can form a double bond;

(xvii) R^{15}, R^{16} and R^{17} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkaryl or aralkyl group, heteroalkyl, heterocycle or heteroaromatic; and

(xviii) R^{100}, R^{101}, R^{102}, R^{103}, and R^{104} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, acyl, heteroaromatic, heteroaryl, heteroalkyl, hydroxyl, alkoxy, cyano, azido, halogen, nitro, SO_2, SO_3, thioalkyl or amino;

(xix) wherein G^1 is not as it is found in natural vitamin B_{12}.

16. (Withdrawn – currently amended) A method for the treatment, prophylaxis and/or diagnosis of a proliferative disorder in a host comprising administering an effective amount of a compound of ~~any one of claims 1-11,~~ a compound of formula (**I**):



or its enantiomer, diastereomer or ~~the~~ pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier, in combination or alternation with one or more other therapeutic and/or diagnostic agent(s), wherein:

(i) the wavy line in the chemical structure indicates either a dative or covalent bond such that there are three dative Co-N bonds and one covalent Co-N bond, wherein, the case of the dative bond, the valence of nitrogen is completed either with a double bond with an adjacent ring carbon or with a hydrogen;

(ii) the dotted line in the chemical structure indicates either a double or single bond such that the double bond does not over-extend the valence of the element (i.e. to give pentavalent carbons) and, in the case of a single bond, the valence is completed with hydrogen;

(iii) X is hydrogen, cyano, halogen, haloalkyl, CF_3, CF_2CF_3, CH_2CF_3, CF_2Cl, NO, NO_2, NO_3, phosphonate, alkyl-$P(O)_2OR^{15}$, $PR^{15}R^{16}R^{17}$, NH_2, $NR^{15}R^{16}$, OH, OR^{15}, SR^{15}, SCN, N_3, $OC(O)R^{15}$, $C(O)_2R^{15}$, $C(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $C(O)_2NR^{15}R^{16}$, $C(O)NR^{15}R^{16}$, $P(O)_2OR^{15}$, $S(O)_2OR^{15}$, a purine or pyrimidine nucleoside or nucleoside analog, adenosyl, 5-FU, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, amino acid, peptide, protein, carbohydrate, heteroalkyl, heterocycle, heteroaryl or alkylheteroaryl;

(iv) M is a monovalent heterocycle or heteroaromatic, which is capable of binding to the adjacent sugar ring, and forming a dative bond with Co^{+3};

(v) K is O, S, NJ^1, C(OH)H, $CR^{100}R^{101}$ or $C(R^{100})V^8Z^8$;

(vi) E is O or S;

(vii) G^1 is alkyl, acyl, silyl, phosphate or L-T;

(viii) Y^1, Y^2, Y^3, Y^4, Y^5, Y^6 and Y^7 independently are O, S or NJ^2;

(ix) V^1, V^2, V^3, V^4, V^5, V^6, V^7 and V^8 independently are O, S, NJ^3, $CR^{102}R^{103}$ or a direct bond;

(x) Z^1, Z^2, Z^3, Z^4, Z^5, Z^7 and Z^8 independently are R^{104} or L-T;

(xi) each L is independently a direct bond or linker to one or more T moieties, and that does not significantly impair the ability of the TC- or IF-binding carrier to bind to a transcobalamin receptor, optionally when bound to a transport protein;

(xii) each T independently comprises the residue of one or more molecules of neutron capture agents;

(xiii) at least one of Z^1, Z^2, Z^3, Z^4, Z^5, Z^7, and Z^8, ~~K and G~~[1] is L-T;

(xiv) J^1, J^2 and J^3 independently are hydrogen, alkyl, alkenyl, alkynyl, alkaryl, cycloalkyl, aryl, cycloaryl, heteroalkyl, heterocycle, heteroaryl, hydroxyl, alkoxy or amine;

(xv) R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} independently are hydrogen, lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, heteroalkyl, heterocyclic, lower alkoxy, azido, amino, lower alkylamino, halogen, thiol, SO_2, SO_3, carboxylic acid, $C_{1\text{-}6}$ carboxyl, hydroxyl, nitro, cyano, oxime or hydrazine;

(xvi) R^{13} and R^{14} optionally can form a double bond;

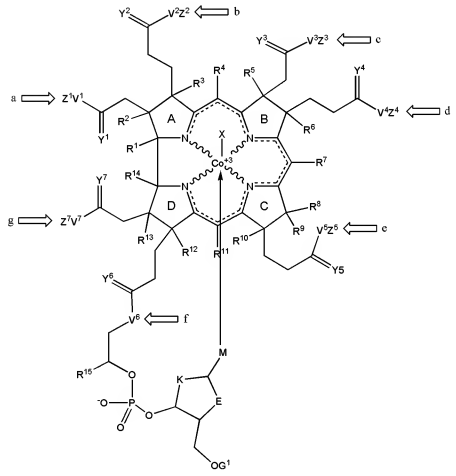
(xvii) R^{15}, R^{16} and R^{17} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkaryl or aralkyl group, heteroalkyl, heterocycle or heteroaromatic; and

(xviii) R^{100}, R^{101}, R^{102}, R^{103}, and R^{104} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, acyl, heteroaromatic, heteroaryl, heteroalkyl, hydroxyl, alkoxy, cyano, azido, halogen, nitro, SO_2, SO_3, thioalkyl or amino;

(xix) wherein G^1 is not as it is found in natural vitamin B_{12}.

17. (Withdrawn) The method of claim 15 or 16, wherein the host is a human.

18. (Withdrawn - currently amended) A method for the treatment, prophylaxis and/or diagnosis of a proliferative disorder other than neoplasms in a host comprising administering an effective amount of a compound of the formula (**I**):



or its enantiomer, diastereomer or its pharmaceutically acceptable salt, wherein:

(i) the wavy line in the chemical structure indicates either a dative or covalent bond such that there are three dative Co-N bonds and one covalent Co-N bond, wherein, the case of the dative bond, the valence of nitrogen is completed either with a double bond with an adjacent ring carbon or with a hydrogen;

(ii) the dotted line in the chemical structure indicates either a double or single bond such that the double bond does not over-extend the valence of the element (i.e. to give pentavalent carbons) and, in the case of a single bond, the valence is completed with hydrogen;

(iii) X is hydrogen, cyano, halogen ~~(Cl, F, Br or I)~~, haloalkyl, CF_3, CF_2CF_3, CH_2CF_3, CF_2Cl, NO, NO_2, NO_3, phosphonate, alkyl-$P(O)_2OR^{15}$, $PR^{15}R^{16}R^{17}$, NH_2, $NR^{15}R^{16}$, OH, OR^{15}, SR^{15}, SCN, N_3, $OC(O)R^{15}$, $C(O)_2R^{15}$, $C(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $C(O)_2NR^{15}R^{16}$, $C(O)NR^{15}R^{16}$, $P(O)_2OR^{15}$, $S(O)_2OR^{15}$, a purine or pyrimidine nucleoside or nucleoside analog, adenosyl, 5-FU, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, amino acid, peptide, protein, carbohydrate, heteroalkyl, heterocycle, heteroaryl or alkylheteroaryl;

(iv) M is a monovalent heterocycle or heteroaromatic, which is capable of binding to the adjacent sugar ring, and forming a dative bond with Co^{+3};

(v) K is O, S, NJ^1, C(OH)H, $CR^{100}R^{101}$ or $C(R^{100})V^8Z^8$;

(vi) E is O or S;

(vii) G^1 is ~~hydrogen,~~ alkyl, acyl, silyl, phosphate or L-T;

(viii) Y^1, Y^2, Y^3, Y^4, Y^5, Y^6 and Y^7 independently are O, S or NJ^2;

(ix) V^1, V^2, V^3, V^4, V^5, V^6, V^7 and V^8 independently are O, S, NJ^3, $CR^{102}R^{103}$ or a direct bond;

(x) Z^1, Z^2, Z^3, Z^4, Z^5, Z^7 and Z^8 independently are R^{104} or L-T;

(xi) each L is independently a direct bond or linker to one or more T moieties, and that does not significantly impair the ability of the TC- or IF-binding carrier to bind to a transcobalamin receptor, optionally when bound to a transport protein;

(xii) each T independently comprises the residue of one or more molecules of neutron capture agents;

(xiii) at least one of Z^1, Z^2, Z^3, Z^4, Z^5, Z^7, and Z^8, ~~K and G^1~~ is L-T;

(xiv) J^1, J^2 and J^3 independently are hydrogen, alkyl, alkenyl, alkynyl, alkaryl, cycloalkyl, aryl, cycloaryl, heteroalkyl, heterocycle, heteroaryl, hydroxyl, alkoxy or amine;

(xv) R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} independently are hydrogen, lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, heteroalkyl, heterocyclic, lower alkoxy, azido, amino, lower alkylamino, halogen, thiol, SO_2, SO_3, carboxylic acid, $C_{1\text{-}6}$ carboxyl, hydroxyl, nitro, cyano, oxime or hydrazine;

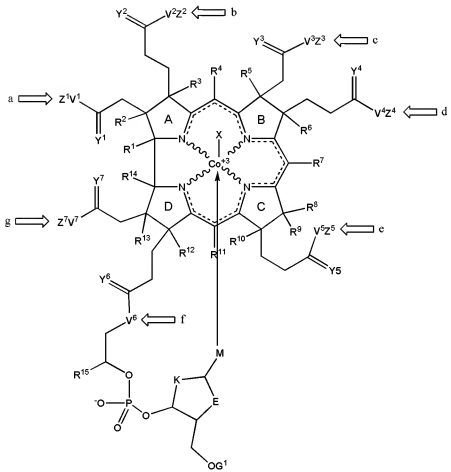
(xvi) R^{13} and R^{14} optionally can form a double bond;

(xvii) R^{15}, R^{16} and R^{17} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkaryl or aralkyl group, heteroalkyl, heterocycle or heteroaromatic; and

(xviii) R^{100}, R^{101}, R^{102}, R^{103}, and R^{104} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, acyl, heteroaromatic, heteroaryl, heteroalkyl, hydroxyl, alkoxy, cyano, azido, halogen, nitro, SO_2, SO_3, thioalkyl or amino;

(xix) wherein G^1 is not as it is found in natural vitamin B_{12}.

19. (Withdrawn – currently amended) A method for the treatment, prophylaxis and /or diagnosis of a proliferative disorder other than neoplasms in a host comprising administering an effective amount of a compound of ~~claim 18,~~ formula (I):



or its enantiomer, diastereomer or ~~the~~ pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier, in combination or alternation with one or more other therapeutic and/or diagnostic agent(s), wherein:

(i) the wavy line in the chemical structure indicates either a dative or covalent bond such that there are three dative Co-N bonds and one covalent Co-N bond,

wherein, the case of the dative bond, the valence of nitrogen is completed either with a double bond with an adjacent ring carbon or with a hydrogen;

(ii) the dotted line in the chemical structure indicates either a double or single bond such that the double bond does not over-extend the valence of the element (i.e. to give pentavalent carbons) and, in the case of a single bond, the valence is completed with hydrogen;

(iii) X is hydrogen, cyano, halogen, haloalkyl, CF_3, CF_2CF_3, CH_2CF_3, CF_2Cl, NO, NO_2, NO_3, phosphonate, alkyl-$P(O)_2OR^{15}$, $PR^{15}R^{16}R^{17}$, NH_2, $NR^{15}R^{16}$, OH, OR^{15}, SR^{15}, SCN, N_3, $OC(O)R^{15}$, $C(O)_2R^{15}$, $C(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $C(O)_2NR^{15}R^{16}$, $C(O)NR^{15}R^{16}$, $P(O)_2OR^{15}$, $S(O)_2OR^{15}$, a purine or pyrimidine nucleoside or nucleoside analog, adenosyl, 5-FU, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, amino acid, peptide, protein, carbohydrate, heteroalkyl, heterocycle, heteroaryl or alkylheteroaryl;

(iv) M is a monovalent heterocycle or heteroaromatic, which is capable of binding to the adjacent sugar ring, and forming a dative bond with Co^{+3};

(v) K is O, S, NJ^1, C(OH)H, $CR^{100}R^{101}$ or $C(R^{100})V^8Z^8$;

(vi) E is O or S;

(vii) G^1 is hydrogen, alkyl, acyl, silyl, phosphate or L-T;

(viii) Y^1, Y^2, Y^3, Y^4, Y^5, Y^6 and Y^7 independently are O, S or NJ^2;

(ix) V^1, V^2, V^3, V^4, V^5, V^6, V^7 and V^8 independently are O, S, NJ^3, $CR^{102}R^{103}$ or a direct bond;

(x) Z^1, Z^2, Z^3, Z^4, Z^5, Z^7 and Z^8 independently are R^{104} or L-T;

(xi) each L is independently a direct bond or linker to one or more T moieties, and that does not significantly impair the ability of the TC- or IF-binding carrier to bind to a transcobalamin receptor, optionally when bound to a transport protein;

(xii) each T independently comprises the residue of one or more molecules of neutron capture agents;

(xiii) at least one of Z^1, Z^2, Z^3, Z^4, Z^5, Z^7, and Z^8, ~~K and G^1~~ is L-T;

(xiv) J^1, J^2 and J^3 independently are hydrogen, alkyl, alkenyl, alkynyl, alkaryl, cycloalkyl, aryl, cycloaryl, heteroalkyl, heterocycle, heteroaryl, hydroxyl, alkoxy or amine;

(xv) R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} independently are hydrogen, lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, heteroalkyl, heterocyclic, lower alkoxy, azido, amino, lower alkylamino, halogen, thiol, SO_2, SO_3, carboxylic acid, $C_{1\text{-}6}$ carboxyl, hydroxyl, nitro, cyano, oxime or hydrazine;

(xvi) R^{13} and R^{14} optionally can form a double bond;

(xvii) R^{15}, R^{16} and R^{17} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkaryl or aralkyl group, heteroalkyl, heterocycle or heteroaromatic; and

(xviii) R^{100}, R^{101}, R^{102}, R^{103}, and R^{104} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, acyl, heteroaromatic, heteroaryl, heteroalkyl, hydroxyl, alkoxy, cyano, azido, halogen, nitro, SO_2, SO_3, thioalkyl or amino;

(xix) wherein G^1 is not as it is found in natural vitamin B_{12}.

20. (Withdrawn – currently amended) The method of claim 18 or 19, wherein at least one T is a molecule ~~that contains~~ comprising B-10.

21. (Withdrawn) The method of claim 20, wherein the molecule that contains B-10 is o-carborane, m-carborane or p-carborane.

22. (Withdrawn – currently amended) The method of claim 18 or 19, wherein at least one T is a molecule ~~that contains~~ comprising Gd-157.

23. (Withdrawn - currently amended) The method of any one of claims 18-22, wherein at least one L is independently an amine, a polyamine, an amino acid, a poly(amino acid) or peptide ~~linker,~~ linker.

24. (Withdrawn) The pharmaceutical composition of any one of claims 18-22, wherein at least one –L-T is independently a poly(amino acid) residue bound to one or more T.

25. (Withdrawn) The method of claim 24, wherein at least one –L-T is independently a poly-L-lysine -NR'$(CH((CH_2)_4$-NHR')CONR'$)_m$R', wherein each R' is independently hydrogen, lower alkyl or T; and m is 2-20.

26. (Withdrawn - currently amended) The method of any one of claims 18-22, wherein at least one -L-T is independently a polyamine residue of the formula -NR'(alkylene-NR')$_n$alkyleneNR'R', wherein each R' is independently hydrogen, lower alkyl ~~or T~~ or T; and n is 1-20.

27. (Withdrawn) The method of claim 26, wherein -NR'(alkylene-NR')$_n$alkyleneNR' is selected from the group consisting of -NR'$(CH_2)_3$NR'$(CH_2)_4$NR'$(CH_2)_3$NR'R'

(spermine); -NR'$(CH_2)_3$NR'$(CH_2)_4$NR'R' (spermidine); decamethylene tetraamine and pentamethylene hexamine.

28. (Withdrawn - currently amended) The method of any one of claims 18-22, wherein at least one -L-T is independently a diamine residue of the formula -NR'(alkylene)$_x$NR'R', wherein each R' is independently hydrogen, lower alkyl ~~or T~~ or T; and x is 2-20.

29. (Withdrawn) The method of claim 28, wherein -NR'(alkylene)$_x$NR'R' is selected from the group consisting of 1,6-diaminohexane, 1,5-diaminopentane, 1,4-diaminobutane and 1,3-diaminopropane.

30. (Withdrawn) The method of any one of claims 18-29, wherein the host is a human.